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EXAMINER

BLANCHARD, DAVID J

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**BEFORE THE BOARD OF PATENT APPEALS
AND INTERFERENCES**

Application Number: 09/835,759

Filing Date: April 16, 2001

Appellant(s): BARBERA-GUILLEM, EMILIO

Scott Harders
For Appellant

EXAMINER'S ANSWER

This is in response to the appeal brief filed 23 December 2005 appealing from the
Office action mailed 26 January 2005.

(1) *Real Party of Interest*

A statement identifying the real party in interest is contained in the brief.

(2) *Related Appeals and Interferences*

The brief contains a statement that there are no related appeals or interferences at this time.

(3) *Status of Claims*

The statement of the status of claims contained in the brief is correct.

(4) *Status of Amendments After Final*

The appellant's statement of the status of amendments after final rejection contained in the brief is correct.

(5) *Summary of Claimed Subject Matter*

The summary of claimed subject matter contained in the brief is correct.

(6) *Grounds of Rejection to be Reviewed on Appeal*

The appellant's statement of the grounds of rejection to be reviewed on appeal is substantially correct. The changes are as follows:

WITHDRAWN REJECTIONS

The following grounds of rejection are not presented for review on appeal because they have been withdrawn by the examiner. The rejection of claims 70-71, 73, 76, 78, 82-84, 86, 89-90, 93-94, 96, 99-100, 105-106, 108 and 111-112 under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement.

(7) *Claims Appendix*

The copy of the appealed claims contained in the Appendix to the brief is correct.

(8) Evidence Relied Upon

Noguchi Y. et al. "Influence of Interleukin 12 on p53 peptide Vaccination Against Established Meth A Sarcoma" Proceedings of the National Academy of Science, USA, vol. 92 (March 1995), pp. 2219-2223.

Trinchieri G. "Interleukin-12 and its role in the Generation of TH1 Cells" Immunology Today, vol. 14, no. 7 (1993), pp. 335-338.

Apostolopoulos V. et al. "Cell-mediated Immune Responses to MUC1 Fusion Protein Coupled to Mannan" Vaccine, vol. 14, no. 9 (1996), pp. 930-938.

Tachibana T. et al. "Tumor Regression in Tumor-Bearing Mice by inoculations of Immunogenic Somatic Hybrid Cells in Combination with Cyclophosphamide" Takai Journal of Experimental Clinical Medicine, vol. 8, no. 5-6 (1983), pp. 455-463.

Parkhouse R. M. E. et al. "Two Surface Antigen Targets for Immunotoxin-Mediated Elimination of Normal and Neoplastic Murine B Cells" Current Topics in Microbiology and Immunology, vol. 182 (1992), pp. 331-335.

5,939,380

WANG

11-1991

(9a) Grounds of Rejection

The following grounds of rejection are applicable to the appealed claims:

Claims 1-2 and 7-10 are rejected under 35 U.S.C 102(b) as being anticipated by Noguchi et al (Proc. Natl. Acad. Sci. USA, 92:2219-2223, 1995) as evidenced by the specification at page 11 and as evidenced by Trinchieri G (Immunology Today, 14(7):335-338, 1993).

The claims are interpreted as being drawn to an immunotherapeutic composition comprising an immunotherapeutic composition for effecting B cell depletion, and a tumor-associated antigen capable of inducing a cell mediated immune response comprising a TH1 response, wherein the immunotherapeutic composition further comprises a component selected from the group consisting of an immunomodulator for inducing a cell mediated immune response comprising a TH1 response, a pharmaceutically acceptable carrier and a combination thereof. For this rejection the intended use as an immunotherapeutic composition for suppressing a TH2 response and for inducing a cell mediated immune response comprising a TH1 response in an individual having a TH2/TH1 imbalance mediated by a disease process comprising a pro-tumor immune response and solid nonlymphoid tumor is given no patentable weight (MPEP 2111.02).

Noguchi et al teach a composition comprising a nonamer p53 peptide (234CM) (i.e., tumor-associated antigen) in QS-21 adjuvant, and IL-12, which is reasonably interpreted as an effector of B cell depletion. As evidenced by the specification at page 11, QS-21 induces a TH1 response, which is known by the skilled artisan (page 11, lines 21-22 of the specification). Therefore, as a property is inherent to a product, QS-21 necessarily induces a TH1 response and is reasonably interpreted as an immunomodulator that induces a TH1 response. Further, as evidenced by Trinchieri, IL-12 induces or promotes a TH1 response and inhibits a TH2 type or humoral/antibody response (see Figures 1 and 2) and is interpreted as an effector of B cell depletion.

Thus, Noguchi et al anticipate the claims as evidenced by the specification at page 11 and as evidenced by Trinchieri.

(10a) Response to Argument

The Brief at page 7 questions the appropriateness of the rejection based on Appellants previous species election (discussed in the first full paragraph at page 5 of the Brief). Appellants assert that based on the species election that the immunotherapeutic composition is being examined to the extent that the immunotherapeutic composition is a monoclonal antibody specific for CD22 and Nogouchi fails to anticipate the claims. This has been fully considered but is not found persuasive for the following reasons. Appellants assertion that the claims are being examined to the extent that the immunotherapeutic composition is a monoclonal antibody specific for CD22 is incorrect. It is respectfully pointed out that the election of species was with respect to the "affinity ligand" recited in dependent claim 5, a claim not rejected as being anticipated (see page 6, item no. 6 of the restriction requirement mailed 11/3/2003). Accordingly, as indicated at page 3, item no. 4 of the non-final Office Action mailed 5/20/2004, the claims are being examined to the extent that the affinity ligand is a monoclonal antibody specific for CD22 (LL2), which was reiterated in the final Office Action mailed 1/26/2005 (see page 2, item no. 2). Thus, the species election only limited the subject matter of claim 5 under examination and given the breadth of the claims and in the interest of compact prosecution, the applicability of the

prior art over the genus claims is deemed appropriate. Further, the timeliness of Appellants query presented in the Brief is curious.

At page 7 of the Brief, Appellants assert that the interpretation of IL-12 as an effector of B cell depletion is incorrect as Trinchieri does not discuss B cells or B cell depletion. Appellant notes that Trinchieri does not show IL-12 acting on B cells, and B cells are not even shown in Figure 1. Appellant concludes that the interpretation of IL-12 as an effector for B cell depletion is incorrect. This has been fully considered but is not found persuasive for the following reasons. First, it is important to note that the claims do not recite any distinguishing structural elements of the “immunotherapeutic composition for effecting B cell depletion” nor do the rejected claims require that the immunotherapeutic composition act directly on B cells with which Appellant argues. Thus, the claims are drawn to some unknown “immunotherapeutic composition” identified solely by its principal biological activity, i.e., effecting B cell depletion. The specification defines B cell depletion broadly at page 8 of the specification, which includes blocking of B cell function, inhibiting the proliferation of B cells, and inhibiting the differentiation of B cells to plasma cells. Appellant is reminded that during patent examination, the claims are given the broadest reasonable interpretation consistent with the specification. See MPEP 904.01. Accordingly, in view of Appellants definition in the specification, Figures 1 and 2 of Trinchieri (the evidence cited by the Examiner), provide extrinsic evidence that IL-12 acts as a negative regulator of TH2 promoting cytokines, such as IL-5, which functions in the proliferation and differentiation of B cells. Appellant acknowledges that TH2 cells support a humoral or antibody mediated immune response

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wherein B cells produce antibodies; antibodies mediate humoral immunity (2nd full paragraph at pg. 5 of the Brief). Therefore, IL-12 inhibition of TH2 promoting cytokines would necessarily inhibit B cell proliferation and differentiation. Thus, as set forth in the rejection, the composition taught by Noguchi et al comprising a nonomer p53 peptide in QS-21 adjuvant and IL-12 reads on the claims as the nonomer p53 peptide is a tumor-associated antigen that is capable of inducing a cell mediated or TH1 immune response and as evidenced by the specification at page 11, QS-21 was known by the skilled artisan to induce a TH1 response and IL-12 is reasonably interpreted as an effector of B cell depletion, in view of the extrinsic evidence of Trinchieri discussed above. Appellant always has the opportunity to amend the claims during prosecution, and broad interpretation by the examiner reduces the possibility that the claim, once issued, will be interpreted more broadly than is justified. *In re Prater*, 415 F.2d 1393, 1404-05, 162 USPQ 541, 550-51 (CCPA 1969). See MPEP 2111.

At the middle of page 7 of the Brief, Appellant states Trinchieri teaches away from the proposition that IL-12 and B cell depletion are equivalent. Appellant summarizes the teachings of Trinchieri as indicating that IL-4 is a major cytokine that is produced during a TH2 or humoral immune response and its effect is dominant over IL-12 and since IL-4 would be present during a TH2 type response, its dominance would preclude any IL-12 activity of the type that would effect B cell depletion. Further, the Brief notes that the examiner previously rejected this argument stating that the intended use of a claimed product carries no patentable weight. Appellant asserts that the examiner has missed the point here. Appellant reiterates their position that IL-12 is not

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an effector of B cell depletion and as such does not anticipate the claims and Appellants arguments have nothing to do with the intended use of the claimed composition. This has been fully considered but is not found persuasive for the following reasons. The examiner acknowledges that Appellants point is that IL-12 is not an effector of B cell depletion. Appellants assert that their arguments have nothing to do with the intended use, while on the other hand Appellant argues the use of the claimed composition during a TH2 or humoral immune response, asserting that IL-12 would not effect B cell depletion because the presence of IL-4 would dominate over IL-12 and preclude any IL-12 activity of the type that would effect B cell depletion. It is reiterated that the intended use of a product claim carries no patentable weight. See MPEP 2111.02. Further, given the absence of any structural elements regarding the “immunotherapeutic composition for effecting B cell depletion”, it is unclear what structural limitations the claim preamble imparts, if any. The claims are drawn to a composition comprising two elements, (1) an immunotherapeutic composition for effecting B cell depletion; and (2) a tumor-associated antigen. In view of the definition at pg. 8 of the specification that deletion used in reference to B cells means among other things, blocking of B cell function, inhibiting the proliferation of B cells, and inhibiting the differentiation of B cells, the art reads on the claims given the broadest reasonable interpretation when read in light of the specification consistent with MPEP 2111. As discussed supra, Noguchi et al teach a composition comprising a nonmer p53 peptide in QS-21 adjuvant and IL-12, which is a composition comprising a tumor-associated antigen capable of inducing a cellular or TH1 response (i.e., p53 in QS-21) and as evidenced by Trinchieri, IL-12

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negatively regulates TH2 promoting cytokines, wherein TH2 cells support a humoral or antibody mediated immune response wherein B cells produce antibodies; antibodies mediate humoral immunity as acknowledged by Appellants.

At page 8 of the Brief, Appellant asserts that the specification teaches away from the proposition that IL-12 can be considered as an effector of B cell depletion. Appellant argues that the specification shows that treatment with anti-mouse IgM plus IL-12 were significantly less effective in preventing recurrence of tumors than the treatment with anti-mouse IgM alone (see Figure 4). Based on the decreased efficacy of the combination of anti-mouse IgM plus IL-12, Appellant concludes that IL-12 is not an effector of B cell depletion. Appellant notes that the examiner previously stated that this argument appears to go more towards enablement of the claimed composition. The Brief states that Appellants argument does not bear on enablement, but is based on a study described in the specification suggesting that IL-12 is not an effector of B cell depletion. Appellant also points out that the paragraph at the top of page 40 of the specification clearly states that the "immunomodulator" is IL-12. This has been fully considered but is not found persuasive for the following reasons. The examiner acknowledges that the instant rejection is based on anticipation and not enablement. Further, it is noted that the disclosure of IL-12 as an immunomodulator is found at page 39, lines 14-15 and 18 and not at the top of page 40. With respect to the experimental evidence in the specification, while the claims are read in light of the specification, limitations from the specification are not read into the claims. See MPEP 2111. Further, the features upon which Appellants rely, i.e., anti-mouse IgM and IL-12 have no

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express basis in the claims. Again, the evidence of Trinchieri, demonstrates that IL-12 negatively regulates or inhibits TH2 promoting cytokines, which promote B cell proliferation and differentiation (i.e., a TH2 or humoral/antibody immune response) and as such IL-12 is reasonably interpreted as an "effector of B cell depletion" in view of Appellants definition at page 8 of the specification and in the absence of any structural limitations of the "immunotherapeutic composition for effecting B cell depletion" that could distinguish over the prior art.

(9b) Grounds of Rejection

Claims 1-5, 7-12, 69-73, 77-78, 80-86, 90, 92-96, 100, 102-108, 112 and 114-115 are rejected under 35 U.S.C. 103(a) as being unpatentable over Apostolopoulos et al (Vaccine, 14(9):930-938, 1996) in view of Tachibana et al (Tokai Journal of Experimental Clinical Medicine 8(5-6):455-463, 1983) and Trinchieri G. (Immunology Today, 14(7):335-338, 1993) and Parkhouse et al (Current Topics in Microbiology and Immunology, 182:331-335) and Wang P. Y-C. (U.S. Patent 5,939,380, filed 1991).

The claims are interpreted as being drawn to an immunotherapeutic composition for suppressing a TH2 response and for inducing a cell mediated immune response (i.e., TH1) in an individual having a TH2/TH1 imbalance mediated by a pro-tumor immune response and solid nonlymphoid tumor comprising a component for effecting B cell depletion, a tumor-associated antigen capable of inducing a cell mediated immune response comprising a TH1 response, wherein the immunotherapeutic composition further comprises a component selected from the group consisting of an

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immunomodulator for inducing a cell mediated immune response comprising a TH1 response, a pharmaceutically acceptable carrier and a combination thereof. The immunotherapeutic composition further comprises an anti-B cell agent and a CD22 monoclonal antibody. The claims are also drawn to the above immunotherapeutic composition for treating a solid nonlymphoid tumor in an individual.

Apostolopoulos et al teach that induction of a humoral immune response (i.e., TH1 response) gives poor tumor protection accompanied by little cellular immunity (i.e., TH2 response), however, when a cellular immune response is induced, this results in significant tumor protection, cytotoxic T lymphocytes and little antibody production (i.e., TH1 or humoral immune response) (see abstract and page 930, right column).

Apostolopoulos et al state "However, in immunotherapy studies mice immunized with either natural mucin (HMFG) or a 20mer synthetic peptide from the VTNR repeat or a MUC1 fusion protein (FP), and challenged with MUC1⁺3T3 cells, had poor tumor protection; significant antibody titers were produced, a detectable CD4⁺ DTH, but no CTL were found." (see page 930, right column). Apostolopoulos et al do not specifically teach an immunotherapeutic composition comprising a component for effecting B cell depletion, a tumor-associated antigen capable of inducing a cell mediated immune response comprising a TH1 response, further comprising a component selected from the group consisting of an immunomodulator for inducing a cell mediated immune response comprising a TH1 response, a pharmaceutically acceptable carrier and a combination thereof and an anti B cell agent and a CD22 monoclonal antibody. These

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deficiencies are made up for in the teachings of Tachibana et al and Trinchieri G. and Parkhouse et al and Wang P. Y-C.

Tachibana et al teach that enhancement of tumor growth was caused by acceleration of the humoral response (i.e., TH2 response; TH2/TH1 imbalance) existing in the tumor bearing state (see page 461 and abstract). Specifically, Tachibana et al teach that in mice with enhanced tumors, the level of immune complexes and antitumor antibodies in sera was more markedly elevated than in sera of untreated tumor-bearers (see abstract). Tachibana et al teach that combined treatment with cyclophosphamide (an immunosuppressant to depress humoral response and/or regulatory cells; see page 456) plus hybrid cells showed no antibody elevation and immune complex production, but generation of potent cytotoxic T cells was comparable to that of immunized hosts and was followed by curative antitumor effect (see page 461).

Trinchieri G. teaches the immunomodulator, IL-12, which induces a cell mediated or TH1 response and negatively regulates or inhibits a TH2 type response (see Figures 1-2).

Parkhouse et al teach that normal B cells bear surface CD22 and an anti-CD22 antibody-ricin conjugate effectively depletes normal B cells (see Figure 3).

Wang P. Y-C. teach solid phase implants for the delivery of biological macromolecules (see entire document).

It would have been prima facie obvious to one of ordinary skill in the art at the time the claimed invention was made to have produced an immunotherapeutic composition for suppressing a TH2 response and inducing a TH1 response comprising

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a component for effecting B cell depletion, a tumor-associated antigen capable of inducing a TH1 response, and a component selected from an immunomodulator for inducing a TH1 response, a pharmaceutical composition or a combination thereof for therapeutic benefit of a solid nonlymphoid tumor.

One of ordinary skill in the art would have been motivated to and had a reasonable expectation of success to have produced an immunotherapeutic composition for suppressing a TH2 response and inducing a TH1 response comprising a component for effecting B cell depletion, a tumor-associated antigen capable of inducing a TH1 response, and a component selected from an immunomodulator for inducing a TH1 response, a pharmaceutical composition or a combination thereof for therapeutic benefit of a solid nonlymphoid tumor in view of Apostolopoulos et al and Tachibana et al and Trinchieri G and Parkhouse et al and Wang P. Y-C because Apostolopoulos et al teach that induction of a humoral immune response (i.e., TH2 response) gives poor tumor protection accompanied by little cellular immunity (i.e., TH1 response), however, when a cellular immune response (TH1) is induced, this results in significant tumor protection, cytotoxic T lymphocytes and little antibody production and Tachibana et al teach that enhancement of tumor growth was caused by acceleration of the humoral response (i.e., TH2 response; TH2/TH1 imbalance) existing in the tumor bearing state. In addition, one of ordinary skill in the art would have been motivated to and had a reasonable expectation of success to have produced an immunotherapeutic composition for suppressing a TH2 response and inducing a TH1 response comprising a component for effecting B cell depletion, a tumor-associated antigen capable of

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inducing a TH1 response, and a component selected from an immunomodulator for inducing a TH1 response, a pharmaceutical composition or a combination thereof for therapeutic benefit of a solid nonlymphoid tumor in view of Apostolopoulos et al and Tachibana et al and Trinchieri G and Parkhouse et al and Wang P. Y-C because Trinchieri G. teaches an immunomodulator, IL-12, which induces a cell mediated or TH1 response and negatively regulates or inhibits a TH2 type response. In addition, one of ordinary skill in the art would have been motivated to and had a reasonable expectation of success to have produced an immunotherapeutic composition for suppressing a TH2 response and inducing a TH1 response comprising a component for effecting B cell depletion, a tumor-associated antigen capable of inducing a TH1 response, and a component selected from an immunomodulator for inducing a TH1 response, a pharmaceutical composition or a combination thereof for therapeutic benefit of a solid nonlymphoid tumor in view of Apostolopoulos et al and Tachibana et al and Trinchieri G and Parkhouse et al and Wang P. Y-C because Parkhouse et al teach that normal B cells bear surface CD22 and an anti-CD22 antibody-ricin conjugate effectively depletes normal B cells and Wang P. Y-C. teach solid phase implants for the delivery of biological macromolecules. Therefore, it would have been obvious to one skilled in the relevant art to produce an immunotherapeutic composition comprising the TH1 immunomodulator, IL-12 as taught by Trinchieri G and an anti-CD22 antibody-ricin conjugate (i.e., anti-B cell agent) for B cell depletion as taught by Parkhouse et al because Apostolopoulos et al teach that induction of a humoral immune response (i.e., TH2 response) gives poor tumor protection, whereas a cellular immune response (i.e.,

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TH1 response) results in significant tumor protection, and Apostolopoulos et al and Tachibana et al high antibody titers (i.e., humoral immune response) correlate with poor tumor protection and it would have been obvious to the skilled artisan to use a solid phase implant to facilitate the administration of the immunotherapeutic composition. Thus, it would have been obvious to one skilled in the art to produce an immunotherapeutic composition for suppressing a TH2 response and inducing a TH1 response comprising a component for effecting B cell depletion, a tumor-associated antigen capable of inducing a TH1 response, and a component selected from an immunomodulator for inducing a TH1 response, a pharmaceutical composition or a combination thereof for therapeutic benefit of a solid nonlymphoid tumor in view of Apostolopoulos et al and Tachibana et al Trinchieri G and Parkhouse et al and Wang P. Y-C.

Therefore, the invention as a whole was *prima facie* obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references.

(10b) Response to Argument

At page 10 of the Brief Appellant asserts that the examiner has failed to establish a *prima facie* case of obviousness based on a lack of motivation to combine the cited references. Appellants state that it is not enough that one can modify a reference in view of a second reference, but rather it is required that one reference suggests the modification of the second reference. Appellants state that it is impermissible to engage hindsight reconstruction of the claimed invention, stating that one cannot use Appellants

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disclosure for choosing distinct elements from the prior art without also showing motivation to combine separate references. At the top of page 11 of the Brief, Appellants state that only Parkhouse et al teach an immunotherapeutic composition for effecting B cell depletion, where an anti-CD22 antibody is conjugated to the cellular toxin, ricin, is taught and there is simply no motivation within Parkhouse, or in the other references, to make the combination proposed by the examiner. This has been fully considered but is not found persuasive. In response to Appellants argument that there is no suggestion to combine the references, the examiner recognizes that references cannot be arbitrarily combined and that there must be some reason why one skilled in the art would be motivated to make the proposed combination of primary and secondary references. In re Nomiya, 184 USPQ 607 (CPA 1975). However, there is no requirement that a motivation to make the modification be expressly articulated. The test for combining references is what the combination of disclosures taken as a whole would suggest to one of ordinary skill in the art. In re McLaughlin, 170 USPQ 209 (CCPA 1971). References are evaluated by what they suggest to one versed in the art, rather than by their specific disclosures. In re Bozek, 163 USPQ 545 (CCPA 1969). In this case, one of ordinary skill in the art would have been motivated and had a reasonable expectation of success at the time the invention was made to modify the teachings of Apostolopoulos et al and produce a composition for inducing a TH1 response in an individual having a TH2/TH1 imbalance associated with a pro-tumor immune response, the composition comprising a tumor-associated antigen (i.e., MUC1) and the anti-CD22 antibody-ricin conjugate of Parkhouse et al for depleting B cells and

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to have placed the composition in a solid phase implant as taught by Wang P. Y-C to facilitate the delivery of the composition for therapeutic benefit of tumors in view of Apostolopoulos et al and Tachibana et al and Trinchieri G and Parkhouse et al and Wang P. Y-C.

The motivation to make the above modifications is made explicit in the teachings of Apostolopoulos et al who teach that induction of a humoral immune response (i.e., TH2 or antibody response) gives poor tumor protection accompanied by little cellular immunity and induction of a cellular immune response (i.e., TH1 response) results in significant tumor protection, cytotoxic T lymphocytes and little antibody production (i.e., TH2 or humoral immune response) (see abstract). Additional motivation for the above modifications and in agreement with Apostolopoulos et al, Tachibana et al state "the enhancement of tumor growth was caused by acceleration of humoral response existing beforehand in the tumor-bearing state" (see pg. 461). Therefore, one of ordinary skill in the art at the time the invention was made would have been motivated to shift the anti-tumor immune response from a humoral/antibody/TH2 immune response existing in the tumor-bearing state to a cellular/TH1 immune response using a composition comprising a B cell depleting agent as taught by Parkhouse et al (i.e., anti-CD22 antibody-ricin conjugate) and a tumor-associated antigen (i.e., MUC1) capable of inducing a TH1 response for tumor therapy because induction of a humoral immune response (TH2/antibody response) gives poor tumor protection accompanied by little cellular immunity, whereas induction of a cellular/TH1 immune response results in significant tumor protection according to Apostolopoulos et al and "the enhancement of tumor

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growth was caused by acceleration of humoral response existing beforehand in the tumor-bearing state” according to Tachibana et al (pg. 461). Further, one of ordinary skill in the art would have had a reasonable expectation of success because Parkhouse et al teach that the anti-CD22 antibody-ricin conjugate effectively eliminated both neoplastic and normal B cells (see Figure 3). Thus, the motivation to combine the B cell depleting agent of Parkhouse et al with a tumor-associated antigen (i.e., MUC-1) is expressed in the teachings of Apostolopoulos et al and Tachibana et al and is not gleaned from appellants disclosure. It must be recognized that any judgment on obviousness is in a sense necessarily a reconstruction based upon hindsight reasoning. But so long as it takes into account only knowledge which was within the level of ordinary skill at the time the claimed invention was made, and does not include knowledge gleaned only from the applicant's disclosure, such a reconstruction is proper. See *In re McLaughlin*, 443 F.2d 1392, 170 USPQ 209 (CCPA 1971).

The Brief at page 11 states that the antibody taught by Parkhouse et al is an anti-CD22 antibody conjugated to the cellular toxin ricin, whereas the present claims recite an anti-CD22 antibody to effect B cell depletion and Appellant states that it might have been obvious to try an anti-CD22 antibody alone to see if B cells could be depleted, however, “obvious to try” is not sufficient to provide motivation to combine references under 35 U.S.C. 103(a). Further, Appellant asserts that there is no reasonable expectation of success that modifying the anti-CD22-ricin conjugate of Parkhouse et al to an anti-CD22 antibody without ricin would effectively deplete B cells. This has been fully considered but is not found persuasive. Contrary to Appellants arguments, the

claims are not limited to an anti-CD22 antibody that is not conjugated to ricin. Independent claims 1 and 9 recite a “composition comprising”, wherein the term “comprising” is inclusive or open-ended and does not exclude additional, unrecited elements. See MPEP 2111.03. Even considering independent claims 69, 82, 92 and 104, which actually recite an anti-CD22 monoclonal antibody, the claims recite a “composition comprising”, which is inclusive or open-ended and does not exclude additional, unrecited elements. Thus, while the recited anti-CD22 antibody is essential, other elements may be added (i.e., ricin conjugate) and still form a construct within the scope of the claims. Appellant does not challenge the motivation or reasonable expectation of success of a composition comprising an anti-CD22-ricin conjugate and a tumor-associated antigen (i.e., MUC-1) as taught by the references.

Appellants argue the specific teachings of Apostolopoulos at page 12 of the Brief stating that Apostolopoulos disclose a particular mannan-conjugated tumor-associated antigen to produce a cell mediated immune response that is effective against tumors, where previous tumor-associated antigens, conjugated to carriers, produced a humoral immune response and inefficient antitumor activity. Appellants assert that Apostolopoulos does not disclose or suggest depleting B cells and there is no teaching or suggestion within Apostolopoulos that humoral immunity could or should be suppressed and there is no motivation to deplete B cells or use an anti-CD22 antibody to deplete B cells. This has been fully considered but is not found persuasive. Appellant is again reminded that references are evaluated by what they suggest to one versed in the art, rather than by their specific disclosures. In re Bozek, 163 USPQ 545

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(CCPA 1969). In response to Appellants argument that there is no teaching or suggestion within Apostolopoulos that humoral immunity could or should be suppressed, it is reiterated that Apostolopoulos teach that induction of a humoral immune response (antibody/TH2 response) mediated by B cells (B cells produce antibodies; antibodies mediate humoral immunity), gives poor tumor protection, whereas induction of a cellular/TH1 immune response results in significant tumor protection, which would have led one of ordinary skill in the art at the time the invention was made to use the anti-CD22 antibody-ricin conjugate for depleting B cells with a reasonable expectation of success in view of the teachings of Parkhouse, providing evidence that the anti-CD22 antibody-ricin conjugate effectively kills neoplastic and normal B cells (see page 334 and Figure 3). Thus, for tumor therapy in individuals having a pro-tumor immune response due to an accelerated humoral immune response, it would have been advantageous to produce a composition comprising an anti-CD22 antibody-ricin conjugate and a tumor-associated antigen to deplete B cells and induce a TH1 immune response, since B cells produce antibodies and mediate humoral immunity (TH2 immune response), which gives poor tumor protection and enhances tumor growth, whereas induction of a cellular/TH1 immune response results in significant tumor protection according to Apostolopoulos and Tachibana et al (discussed supra). The strongest rationale for combining references is a recognition, expressly or impliedly in the prior art or drawn from a convincing line of reasoning based on established scientific principles or legal precedent, that some advantage or expected beneficial

result would have been produced by their combination. In re Sernaker, 702 F.2d 989, 994-95, 217 USPQ 1, 5-6 (Fed. Cir. 1983). See MPEP 2144.

At page 12 of the Brief, Appellant argues that the teachings of Tachibana indicating that humoral immune responses inhibit cell mediated antitumor activity is not the same as suggesting depletion of B cells or depletion of B cells with an anti-CD22 antibody to eliminate a humoral immune response and Appellant argues that one would not have been motivated to combine Tachibana with Parkhouse to come up with a composition containing an anti-CD22 antibody that alone is sufficient to deplete B cells. Appellant reiterates that the anti-CD22 antibody of Parkhouse is conjugated to ricin and argues an “obvious to try” standard, stating that something obvious to try is not sufficient motivation to combine or modify a reference. This has been fully considered but is not found persuasive. As discussed above, the anti-CD22 antibody-ricin conjugate of Parkhouse reads on the claims because the claims are not limited to an anti-CD22 antibody that is not conjugated to ricin. Again, Appellant is reminded that the term “comprising” is inclusive or open-ended and does not exclude additional, unrecited elements (MPEP 2111.03). While the recited anti-CD22 antibody is essential, other elements may be added (i.e., ricin conjugate) and still form a construct within the scope of the claims.

The Examiner acknowledges Appellants citation of Lord et al at the bottom of pg. 11 of the Brief, however, the evidence is not supplied and has not been considered and the deletion of the citation at page 11 of the Appeal Brief appears to be an oversight by Appellant in response to the notice of Non-Complaint Appeal Brief mailed 9/21/2005.

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(11) Related Proceeding(s) Appendix

No decision rendered by a court or the Board is identified by the examiner in the Related Appeals and Interferences section of this examiner's answer.

For the above reasons, it is believed that the rejections should be sustained.

Respectfully submitted,

David J. Blanchard



Conferees:

Larry R. Helms, SPE AU 1643



**LARRY R. HELMS, PH.D.
SUPERVISORY PATENT EXAMINER**

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